

## **REMARKS/ARGUMENTS**

### **I. STATUS**

#### **A. SPECIFICATION**

The specification was amended to correct typographical errors.

#### **B. CLAIMS**

Claims 14, 15, 17 – 27, 41 – 4, 45, 46, 49 – 51 and 54 - 69 are pending and under examination.

Claim 15 was amended to include the subject matter of claim 16.

Claims 41 and 42 were re-written in independent form.

Claim 43 was amended to depend from claim 15.

Claim 50 was amended to depend from claim 41.

Claims 54 through 69 were added. Support for new claims 54 and 55 can be found in claim 17.

Support for new claims 56, 64 and 67 can be found in claim 49.

Support for new claim 57 can be found in claim 23.

Support for new claims 58 and 68 can be found in claim 45.

Support for new claims 59 and 69 can be found in claim 46.

Support for new claims 60 and 62 can be found in claim 15.

Support for new claims 61 and 63 can be found in claim 43.

Support for new claim 65 can be found in claim 21.

Support for new claim 66 can be found in claim 51

Claims 16, 28 – 34, 38 – 40, 44, 47 – 48 and 52 – 53 were cancelled herein.

Cancellation of subject matter is without prejudice to subsequent revival for prosecution in a divisional or continuation application.

The amendments are fully supported by the application as filed and do not introduce new matter. Entry of this amendment is respectfully requested.

### **II. WITHDRAWAL OF REJECTIONS**

Applicants thank the Examiner for the withdrawal of the following rejections.

- Claims 14 and 17–18 under 35 U.S.C. § 102(e) as anticipated by Agnew *et*

*al.*

- Claims 14, 17–20, 22–24, 26–28, 41–42 and 49–53 under 35 U.S.C. § 102(b) as anticipated by Zimmerman *et al.*
- Claims 15 – 16 and 43 – 48 under 35 U.S.C. § 103(a) as unpatentable over Zimmerman or Agnew, in view of Gobom *et al.*
- Claim 21 under 35 U.S.C. § 103(a) as unpatentable over Zimmerman
- Claim 25 under 35 U.S.C. § 103(a) as unpatentable over Zimmerman in view of Agnew.
- Claims 26–27 under 35 U.S.C. § 103(a) as unpatentable over Zimmerman in view of Strosberg *et al.*

### **III. ALLOWABLE SUBJECT MATTER**

Applicants thank the Examiner for thoroughly reviewing the art and finding allowable subject matter.

### **IV. REJECTIONS UNDER 35 U.S.C. § 103(a)**

#### **A. CHAN OR YU IN VIEW OF HEEGAARD OR YU**

Claims 14, 17 – 21, 23, 26 – 28 and 43 – 53 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Chan (Biochemistry **2000**, 39, 7221 – 7228, “Chan”) or Yu (Biochemistry **2001**, 40, 15581 – 15590, “Yu-B”) in view of Heegaard (Journal of Chromatography B, 715 (1998) 29 – 54, “Heegaard”) or Yu (Anal. Chem. **2001**, 73, 5088 – 5096, “Yu-A”). Applicants respectfully traverse the rejection.

The instant claims are directed to methods for capturing and dissecting a multi-protein complex in an open extraction channel. In particular, independent claim 14 is drawn to a method for extracting a multi-protein complex. Applicants define multiprotein complexes as a complex of two or more proteins held together by mutually attractive chemical forces, typically non-covalent interactions<sup>1</sup>. In the above definition, Applicants are referring to two or more **different** proteins.

The Examiner is relying on Chan and Yu-B to teach purification of multi-protein complexes. The Examiner is using the term, “protein complex” to refer to the proteins taught by

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<sup>1</sup> Applicants’ specification, page 57, lines 12-14.

Chan and Yu-B. It is Applicants' position that Chan and Yu-B do not teach purification of **multi**-protein complexes comprised of two or more **different** proteins. Instead, Chan and Yu-B teach purification of single proteins that contain more than one subunit. The Fe protein taught by Chan is a heterodimer, comprised of two 30-kd subunits<sup>2</sup>. The argininosuccinate lyase enzyme purified by Yu-B is also a single protein, a tetramer of four subunits<sup>3</sup>.

In contrast to the teachings of Chan and Yu-B, the instant claims are directed to **multi**-protein complexes. According to Merriam-Webster's Dictionary of Prefixes, Suffixes, and Combining Forms, the prefix, "multi" describes multiple or more than one<sup>4</sup>. Furthermore, the multi-protein complexes listed in the following passage from Applicants' specification are comprised of tens, if not hundreds of **different** proteins<sup>5</sup> (bold emphasis added).

Because of the nature of the capillaries, which are not as susceptible to clogging, unswept dead volumes or sample loss as conventional packed chromatography columns, they can be used for processing very large biological complexes, including large **multiprotein complexes such as ribosomes, transcription complexes, proteasomes**, etc., as well as organelles, membranes, viruses and whole cells.

In summary, independent claim 14 is drawn to methods for purifying a multi-protein complex made up of at least two proteins while Chan and Yu-B both teach purification of a single protein comprised of multiple subunits. If the Examiner takes issue with the term, "multi-protein complex", Applicants would welcome the opportunity to work with the Examiner to identify suitable claim language to describe the instant invention.

Therefore, claim 14 is not obvious over the combination of Chan, Yu-B, Heegaard and Yu-A. Since claims 17 – 21, 23, 26, 27, 43, 45, 46, 49 - 51 all depend from claim 14, and thus further limit claim 14, claims 17 – 21, 23, 26, 27, 43, 45, 46 and 49 – 51 are not obvious over the combination of Chan, Yu-B, Heegaard and Yu-A. Claims 28, 44, 47, 48, 52 and 53 were cancelled herein, rendering the rejections moot. In view of the foregoing, the withdrawal of the rejections under 35 U.S.C. § 103(a) is respectfully requested.

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<sup>2</sup> Chan, page 7221, left column and Figure 1.

<sup>3</sup> Yu-B, page 1639, right column.

<sup>4</sup> <http://www.scribd.com/doc/240281/MerriamWebsters-a-Dictionary-of-Prefixes-Suffixes-And-Combining-Forms>

<sup>5</sup> Applicants' specification, page 9, line 29 through page 10, line 2.

**B. CHAN OR YU-B IN VIEW OF HEEGAARD OR YU-A IN VIEW OF BOETTGER OR GOBOM**

Claims 15 and 16 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Chan or Yu-B in view of Heegaard or Yu-A as applied to claim 14 above, and further in view of Boettger (US 4,221,568, “Boettger”) or Gobom. Applicants respectfully traverse the rejection.

The Examiner states, “It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify Chan or Yu-B by purging the channel with gas before adding the desorption solution in order to gain the predictable results of a smooth and continuous liquid flow during the purification of the protein as taught by Gobom or to increase the efficiency of the process as taught by Boettger.”

Claim 15 depends from claim 14 and is drawn to a method of purging the extraction channel with a gas prior to desorption. The Examiner is relying on Chan or Yu-B to teach the subject matter of claim 14, extraction of a multi-protein complex. However, as Applicants argued above in section A, neither Chan nor Yu-B teach the method of claim 14.

Boettger or Gobom do not supply the missing teachings. Boettger teaches a sample processor for chemical analysis. Boettger does not teach methods for extracting multi-protein complexes. Gobom teaches a nano-scale reversed-phase column to prepare samples for MALDI/MS. Gobom uses the column on peptides such as a tryptic digest of bovine serum albumin and a peptide mixture<sup>6</sup>. Gobom does not teach methods for extracting multi-protein complexes.

Therefore, claim 15 is not obvious of the combination of Chan, Yu-B, Heegaard, Yu-A and Boettger or Gobom. Claim 16 was cancelled herein, however the subject matter of claim 16 was incorporated into claim 15. In view of the foregoing, the withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

**C. CHAN OR YU-B IN VIEW OF HEEGAARD OR YU-A IN FURTHER VIEW OF BORNHORST.**

Claims 22 and 24 - 25 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Chan or Yu-B in view of Heegaard or Yu-A as applied to claims 19 - 20 above, and further in view of Bornhorst (Methods in Enzymology, 2001, “Bornhorst”). Applicants respectfully traverse the rejection.

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<sup>6</sup> Gobom, page 110, left column, page 111, Figure 4, legend and page 111, left column.

The Examiner states, “It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate an agent such as urea or guanidine hydrochloride into the desorption solutions of Chan or Yu-B because as taught by Bornhorst there are situations in which protein purification requires the protein-protein interactions to be removed in order to facilitate the purification using a polyhistidine affinity tag.”

Claims 22, 24 and 25 all depend (indirectly) from claim 14 and are drawn to methods of dissociating the multi-protein complex. The Office is relying on Chan or Yu-B to teach the subject matter of claim 14, extraction of a multi-protein complex. However, as Applicants argued above in section A, neither Chan nor Yu-B teach the method of claim 14.

Bornhorst does not supply the missing teachings. Bornhorst teaches methods for expression and purification of single proteins (such as membrane proteins or ERK2 protein<sup>7</sup>) using polyhistidine tags using immobilized metal affinity chromatography. Bornhorst does not teach methods for extracting complexes comprised of multiple proteins.

Therefore, claim 14 is not obvious of the combination of Chan, Yu-B, Heegaard, Yu-A and Bornhorst. Since claims 22, 24 and 25 depend from claim 14, claims 22, 24 and 25 are not obvious of the combination of Chan, Yu-B, Heegaard, Yu-A and Bornhorst. In view of the foregoing, the withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

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<sup>7</sup> Bornhorst, page 249 and page 251.

**CONCLUSION**

Entry of this Amendment is respectfully requested. An early and favorable action on the merits is earnestly solicited.

The Commissioner is hereby authorized to charge \$245 for a two-month extension of time to Deposit Account No. 50-2852. In the event that an extension of time is required in addition to that requested, the Commissioner is requested to grant that extension of time, which is required to make this response timely. The Commissioner is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. 50-2852.

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (408) 267-7214.

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Respectfully submitted,

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